

SEQUENCE LISTING

- (1) GENERAL INFORMATION:
 - (i) APPLICANT: RUEGER, David C. TUCKER, Marjorie M.
 - (ii) TITLE OF INVENTION: IMPROVED OSTEOGENIC DEVICES AND METHODS OF USE THEREOF FOR REPAIR OF ENDOCHONDRAL BONE AND OSTEOCHONDRAL DEFECTS
 - (iii) NUMBER OF SEQUENCES: 9
 - (iv) CORRESPONDENCE ADDRESS:
 (A) ADDRESSEE: CREATIVE BIOMOLECULES, INC
 (B) STREET: 45 SOUTH STREET

 - (C) CITY: HOPKINTON
 (D) STATE: MA
 (E) COUNTRY: USA

 - (F) ZIP: 01748
 - (v) COMPUTER READABLE FORM:

 - (A) MEDIUM TYPE: Floppy disk
 (B) COMPUTER: IBM PC compatible
 (C) OPERATING SYSTEM: PC-DOS/MS-DOS
 - (D) SOFTWARE: PatentIn Release #1.0, Version #1.30
 - (vi) CURRENT APPLICATION DATA:
 (A) APPLICATION NUMBER:
 (B) FILING DATE:

 - (C) CLASSIFICATION:
 - - (ix) TELECOMMUNICATION INFORMATION:
 (A) TELEPHONE: (617) 248-7000
 (B) TELEFAX: (617) 248-7100
- (2) INFORMATION FOR SEQ ID NO:1:
 - (i) SEQUENCE CHARACTERISTICS:

 (A) LENGTH: 1822 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single

 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: cDNA
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: HOMO SAPIENS -(-F-)-TISSUE-TYPE:-HIPPOCAMPUS-
 - (ix) FEATURE:

 - EATURE:
 (A) NAME/KEY: CDS
 (B) LOCATION: 49..1341
 (C) IDENTIFICATION METHOD: experimental
 (D) OTHER INFORMATION: /function= "OSTEOGENIC PROTEIN"

/standard_name= "OP1'

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1: GGTGCGGGCC CGGAGCCCGG AGCCCGGGTA GCGCGTAGAG CCGGCGCG ATG CAC GTG Met His Val CGC TCA CTG CGA GCT GCG GCG CCG CAC AGC TTC GTG GCG CTC TGG GCA Arg Ser Leu Arg Ala Ala Ala Pro His Ser Phe Val Ala Leu Trp Ala 5 10 15 105 CCC CTG TTC CTG CTG CGC TCC GCC CTG GCC GAC TTC AGC CTG GAC AAC Pro Leu Phe Leu Leu Arg Ser Ala Leu Ala Asp Phe Ser Leu Asp Asn 20 30 35 153 GAG GTG CAC TCG AGC TTC ATC CAC CGG CGC CTC CGC AGC CAG GAG CGG Glu Val His Ser Ser Phe Ile His Arg Arg Leu Arg Ser Gln Glu Arg 40201 CGG GAG ATG CAG CGC GAG ATC CTC TCC ATT TTG GGC TTG CCC CAC CGC Arg Glu Met Gln Arg Glu Ile Leu Ser Ile Leu Gly Leu Pro His Arg 60 65 249 CCG CGC CCG CAC CTC CAG GGC AAG CAC AAC TCG GCA CCC ATG TTC ATG Pro Arg Pro His Leu Gln Gly Lys His Asn Ser Ala Pro Met Phe Met 70 75 80297 CTG GAC CTG TAC AAC GCC ATG GCG GTG GAG GAG GGC GGC GGC CCC GGC Leu Asp Leu Tyr Asn Ala Met Ala Val Glu Glu Gly Gly Pro Gly 85 90 95 345 GGC CAG GGC TTC TCC TAC CCC TAC AAG GCC GTC TTC AGT ACC CAG GGC Gly Gln Gly Phe Ser Tyr Pro Tyr Lys Ala Val Phe Ser Thr Gln Gly 100 105 110 115393 CCC CCT CTG GCC AGC CTG CAA GAT AGC CAT TTC CTC ACC GAC GCC GAC Pro Pro Leu Ala Ser Leu Gln Asp Ser His Phe Leu Thr Asp Ala Asp 120 125 130441 ATG GTC ATG AGC TTC GTC AAC CTC GTG GAA CAT GAC AAG GAA TTC TTC Met Val Met Ser Phe Val Asn Leu Val Glu His Asp Lys Glu Phe Phe 489 CAC CCA CGC TAC CAC CAT CGA GAG TTC CGG TTT GAT CTT TCC AAG ATC His Pro Arg Tyr His His Arg Glu Phe Arg Phe Asp Leu Ser Lys Ile 150 155 160537 CCA GAA GGG GAA GCT GTC ACG GCA GCC GAA TTC CGG ATC TAC AAG GAC Pro Glu Gly Glu Ala Val Thr Ala Ala Glu Phe Arg Ile Tyr Lys Asp 165 170 175585 TAC ATC CGG GAA CGC TTC GAC AAT GAG ACG TTC CGG ATC AGC GTT TAT Tyr Ile Arg Glu Arg Phe Asp Asn Glu Thr Phe Arg Ile Ser Val Tyr 180 185 190 190633 CAG GTG CTC CAG GAG CAC TTG GGC AGG GAA TCG GAT CTC TTC CTG CTC
-Gln-Val-Leu-Gln-Glu-His-Leu-Gly-Arg-Glu-Ser-Asp-Leu-Phe-Leu-Leu200 205 210 681 GAC AGC CGT ACC CTC TGG GCC TCG GAG GAG GGC TGG CTG GTG TTT GAC Asp Ser Arg Thr Leu Trp Ala Ser Glu Glu Gly Trp Leu Val Phe Asp 215 220 225729 ATC ACA GCC ACC AGC AAC CAC TGG GTG GTC AAT CCG CGG CAC AAC CTG Ile Thr Ala Thr Ser Asn His Trp Val Val Asn Pro Arg His Asn Leu 230 240777

GGC CTG CAG CTC TCG GTG GAG ACG CTG GAT GGG CAG AGC ATC AAC CCC Gly Leu Gln Leu Ser Val Glu Thr Leu Asp Gly Gln Ser Ile Asn Pro 245 250 250

825



AAG Lys 260	TTG Leu	GCG Ala	GGC Gly	CTG Leu	ATT Ile 265	GGG Gly	CGG Arg	CAC His	GGG Gly	CCC Pro 270	CAG Gln	AAC Asn	AAG Lys	CAG Gln	CCC Pro 275	873
	ATG Met	GTG Val	GCT Ala	TTC Phe 280	TTC Phe	AAG Lys	GCC Ala	ACG Thr	GAG Glu 285	GTC Val	CAC His	TTC Phe	CGC Arg	AGC Ser 290	ATC Ile	921
CGG Arg	TCC Ser	ACG Thr	GGG Gly 295	AGC Ser	AAA Lys	CAG Gln	CGC Arg	AGC Ser 300	CAG Gln	AAC Asn	CGC Arg	TCC Ser	AAG Lys 305	ACG Thr	CCC Pro	969
AAG Lys	AAC Asn	CAG Gln 310	GAA Glu	GCC Ala	CTG Leu	CGG Arg	ATG Met 315	GCC Ala	AAC Asn	GTG Val	GCA Ala	GAG Glu 320	AAC Asn	AGC Ser	AGC Ser	1017
AGC Ser	GAC Asp 325	CAG Gln	AGG Arg	CAG Gln	GCC Ala	TGT Cys 330	AAG Lys	AAG Lys	CAC His	GAG Glu	CTG Leu 335	TAT Tyr	GTC Val	AGC Ser	TTC Phe	1065
CGA Arg 340	Asp	CTG Leu	GGC Gly	TGG Trp	CAG Gln 345	GAC Asp	TGG Trp	ATC Ile	ATC Ile	GCG Ala 350	CCT Pro	GAA Glu	GGC Gly	TAC Tyr	GCC Ala 355	1113
GCC Ala	TAC Tyr	TAC Tyr	TGT Cys	GAG Glu 360	GGG Gly	GAG Glu	TGT Cys	GCC Ala	TTC Phe 365	FIO	CTG Leu	AAC Asn	TCC Ser	TAC Tyr 370	ATG Met	1161
AAC Asn	GCC Ala	ACC Thr	AAC Asn 375	His	GCC Ala	ATC Ile	GTG Val	CAG Gln 380	. 1111	CTG Leu	GTC Val	CAC His	TTC Phe 385		AAC Asn	1209
CCG Pro	GAA Glu	ACG Thr 390	Val	CCC Pro	AAG Lys	CCC	TGC Cys 395	Cys	GCG Ala	CCC Pro	ACG Thr	CAG Gln 400		AAT Asn	GCC Ala	1257
ATC Ile	TCC Ser 405	. Val	CTC Lev	TAC Tyr	TTC Phe	GAT Asp 410	ASL	AGC Ser	TCC Ser	AAC Asn	GTC Val 415		CTG Leu	AAG Lys	AAA Lys	1305
TAC Tyr 420	: Arg	AAC Asr	ATC Met	GTG Val	GTC Val 425	. Arg	GCC Ala	TGT Cys	GG(Gl _y	TGC Cys 430	, ,,,,,,,	TAG	CTCC	TCC		1351
GAC	TAA	CAG	ACCO	TTTC	GG (CCA	AGTTI	T T	CTGG	ATCCI	CCA	ATTG(CTCG	CCTT	rGGCCAG	1411
GAGAATTCAG ACCCTTTGGG GCCAAGTTTT TCTGGATCCT CCATTGCTCG CCTTGGCCAG GAACCAGCAG ACCAACTGCC TTTTGTGAGA CCTTCCCCTC CCTATCCCCA ACTTTAAAGG														1471		
																1531
TGTGAGAGTA TTAGGAAACA TGAGCAGCAT ATGGCTTTTG ATCAGTTTTT CAGTGGCAGC ATCCAATGAA CAAGATCCTA CAAGCTGTGC AGGCAAAACC TAGCAGGAAA AAAAAACAAC														1591		
																1651
GCATAAAGAA AAATGGCCGG GCCAGGTCAT TGGCTGGGAA GTCTCAGCCA TGCACGGACT														1711		
															GAAGTTC	1771
				CACA												1822
CI	GIAA	·	101													

(2) INFORMATION FOR SEQ ID NO:2:

- (i) SEQUENCE CHARACTERISTICS:

 (A) LENGTH: 431 amino acids
 (B) TYPE: amino acid
 (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: protein



(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2: Met His Val Arg Ser Leu Arg Ala Ala Ala Pro His Ser Phe Val Ala Leu Trp Ala Pro Leu Phe Leu Leu Arg Ser Ala Leu Ala Asp Phe Ser 20 25 30Leu Asp Asn Glu Val His Ser Ser Phe Ile His Arg Arg Leu Arg Ser $\frac{1}{40}$ Gln Glu Arg Arg Glu Met Gln Arg Glu Ile Leu Ser Ile Leu Gly Leu 50 60Pro His Arg Pro Arg Pro His Leu Gln Gly Lys His Asn Ser Ala Pro 65 70 80 Met Phe Met Leu Asp Leu Tyr Asn Ala Met Ala Val Glu Glu Gly Gly 95 Gly Pro Gly Gly Gln Gly Phe Ser Tyr Pro Tyr Lys Ala Val Phe Ser 100 105 110Thr Gln Gly Pro Pro Leu Ala Ser Leu Gln Asp Ser His Phe Leu Thr 115 120 125 Asp Ala Asp Met Val Met Ser Phe Val Asn Leu Val Glu His Asp Lys 130 140 Glu Phe Phe His Pro Arg Tyr His His Arg Glu Phe Arg Phe Asp Leu 145 150 160 Ser Lys Ile Pro Glu Gly Glu Ala Val Thr Ala Ala Glu Phe Arg Ile 165 170 175Tyr Lys Asp Tyr Ile Arg Glu Arg Phe Asp Asn Glu Thr Phe Arg Ile 180 185 Ser Val Tyr Gln Val Leu Gln Glu His Leu Gly Arg Glu Ser Asp Leu 195 200 205 Phe Leu Leu Asp Ser Arg Thr Leu Trp Ala Ser Glu Glu Gly Trp Leu 210 220 Val Phe Asp Ile Thr Ala Thr Ser Asn His Trp Val Val Asn Pro Arg 225 230 240 His Asn Leu Gly Leu Gln Leu Ser Val Glu Thr Leu Asp Gly Gln Ser 245 250 255 Ile Asn Pro Lys Leu Ala Gly Leu Ile Gly Arg His Gly Pro Gln Asn 260 265 Lys Gln Pro Phe Met Val Ala Phe Phe Lys Ala Thr Glu Val His Phe

Arg
290Ser
290Ile
ArgArgSer
295Ile
295LysGln
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AlaLeu
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Ser Tyr Met Asn Ala Thr Asn His Ala Ile Val Gln Thr Leu Val His 370 380

Phe Ile Asn Pro Glu Thr Val Pro Lys Pro Cys Cys Ala Pro Thr Gln 385 390 395 400

Leu Asn Ala Ile Ser Val Leu Tyr Phe Asp Asp Ser Ser Asn Val Ile 405 410 415

Leu Lys Lys Tyr Arg Asn Met Val Val Arg Ala Cys Gly Cys His 420 425 430

- (2) INFORMATION FOR SEQ ID NO:3:
 - (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 102 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS:

 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (ix) FEATURE:

 - (A) NAME/KEY: Protein
 (B) LOCATION: 1..102

(D) OTHER INFORMATION: /label= OPX

/note= "wherein each Xaa is independently selected from a group of one or more specified amino acids as defined in the specification."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

Cys Xaa Xaa His Glu Leu Tyr Val Xaa Phe Xaa Asp Leu Gly Trp Xaa 1 10 15

Asp Trp Xaa Ile Ala Pro Xaa Gly Tyr Xaa Ala Tyr Tyr Cys Glu Gly 20 30

Glu Cys Xaa Phe Pro Leu Xaa Ser Xaa Met Asn Ala Thr Asn His Ala 35 40 45

Ile Xaa Gln Xaa Leu Val His Xaa Xaa Xaa Pro Xaa Xaa Val Pro Lys 50 60

Xaa Cys Cys Ala Pro Thr Xaa Leu Xaa Ala Xaa Ser Val Leu Tyr Xaa 65 75 80

Asp Xaa Ser Xaa Asn Val Xaa Leu Xaa Lys Xaa Arg Asn Met Val Val 90 95

Xaa Ala Cys Gly Cys His 100

- (2) INFORMATION FOR SEQ ID NO:4:
 - (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 97 amino acids
 (B) TYPE: amino acid

 - (C) STRANDEDNESS:
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (ix) FEATURE:
 - (A) NAME/KEY: Protein (B) LOCATION: 1..97

(D) OTHER INFORMATION: /label= Generic-Seq-7 /note= "wherein each Xaa is independently selected from a group of one or more specified amino acids as defined in the specification."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

Leu Xaa Xaa Xaa Phe Xaa Xaa Xaa Gly Trp Xaa Xaa Xaa Xaa Xaa Xaa 1 15

Pro Xaa Xaa Xaa Ala Xaa Tyr Cys Xaa Gly Xaa Cys Xaa Xaa Pro 25 30

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Asn His Ala Xaa Xaa Xaa Xaa Xaa 35

Val Xaa Leu Xaa Xaa Xaa Xaa Met Xaa Val Xaa Xaa Cys Xaa Cys

Xaa

(2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 102 amino acids
(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:

(A) NAME/KEY: Protein (B) LOCATION: 1..102

(D) OTHER INFORMATION: /label= Generic-Seq-8 /note= "wherein each Xaa is independently selected from a group of one or more specified amino acids as defined in the specification."

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

Cys Xaa Xaa Xaa Xaa Leu Xaa Xaa Xaa Phe Xaa Xaa Gly Tr
p Xaa 1 10 15 15

Xaa Xaa Xaa Xaa Pro Xaa Xaa Xaa Ala Xaa Tyr Cys Xaa Gly 20 25 30

Xaa Cys Xaa Xaa Pro Xaa Xaa Xaa Xaa Xaa Xaa Xaa Asn His Ala 35 40 45

Xaa Cys Cys Xaa Pro Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Leu Xaa Xaa 70

Xaa Xaa Xaa Xaa Val Xaa Leu Xaa Xaa Xaa Xaa Xaa Met Xaa Val 85 90 95

Xaa Xaa Cys Xaa Cys Xaa 100

- (2) INFORMATION FOR SEQ ID NO:6:
 - (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 97 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single

 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein

 - (ix) FEATURE:

 (A) NAME/KEY: Protein

 (B) LOCATION: 1..97

 (D) OTHER INFORMATION: /label= Generic-Seq-9

 /note= "wherein each Xaa is independently selected from a group of one or more specified amino acids as defined in the specification."
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

Pro Xaa Xaa Xaa Xaa Xaa Xaa Cys Xaa Gly Xaa Cys Xaa Xaa Xaa 20 25

Xaa

- (2) INFORMATION FOR SEQ ID NO:7:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 102 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: protein
 - (ix) FEATURE:
 - (A) NAME/KEY: Protein
 (B) LOCATION: 1..102
 (D) OTHER INFORMATION: /label= Generic-Seq-10 /note= "wherein each Xaa is independently selected from a group of one or more specified amino acids as defined in the specification."
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

N Ø m Xaa Xaa Xaa Xaa Aaa Pro Xaa Xaa Xaa Xaa Xaa Xaa Cys Xaa Gly 20 25 30

Xaa Xaa Cys Xaa Pro Xaa Xaa Xaa Xaa Xaa Xaa Xaa Leu Xaa Xaa 65 70 80

Xaa Xaa Cys Xaa Cys Xaa 100

- (2) INFORMATION FOR SEQ ID NO:8:
 - (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 5 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS:

 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (ix) FEATURE:
 - (A) NAME/KEY: Protein
 (B) LOCATION: 1..5
 (D) OTHER INFORMATION: /note= "wherein each Xaa is independently selected from a group of one or more specified amino acids as defined in the specification"
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

Cys Xaa Xaa Xaa Xaa 1 5

- (2) INFORMATION FOR SEQ ID NO:9:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 5 amino acids
 (B) TYPE: amino acid
 - STRANDEDNESS:
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
 - (ix) FEATURE:
 - (A) NAME/KEY: Protein

 (B) LOCATION: 1..5

 (D) OTHER INFORMATION: /note= "wherein each Xaa is independently selected from a group of one or more specified amino acids as defined in the specification"
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

Cys Xaa Xaa Xaa Xaa